



PCT09

## RAW SEQUENCE LISTING

DATE: 02/06/2002

PATENT APPLICATION: US/09/647,780A

TIME: 14:14:29

Input Set : A:\PTO.VSK.txt

Output Set: N:\CRF3\02062002\I647780A.raw

ENTERED

5 <110> APPLICANT: OUIMET et al.

7 <120> TITLE OF INVENTION: Novel membrane-bound metalloprotease NEP II and the use thereof for

8 screening inhibitors useful in therapy

10 <130> FILE REFERENCE: P06910US0/BAS

C--> 12 <140> CURRENT APPLICATION NUMBER: US/09/647,780A

C--> 13 <141> CURRENT FILING DATE: 2001-12-13

15 <150> PRIOR APPLICATION NUMBER: PCT/FR99/00807

16 <151> PRIOR FILING DATE: 1999-04-07

18 <150> PRIOR APPLICATION NUMBER: FR/9804389

19 <151> PRIOR FILING DATE: 1998-04-08

21 <160> NUMBER OF SEQ ID NOS: 29

23 <170> SOFTWARE: PatentIn Ver. 2.1

25 <210> SEQ ID NO: 1

26 <211> LENGTH: 2765

27 <212> TYPE: DNA

28 <213> ORGANISM: Rattus rattus

30 <220> FEATURE:

31 <221> NAME/KEY: CDS

32 <222> LOCATION: (107) ... (2428)

34 <400> SEQUENCE: 1

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37 ctggccctgg gtgctcagct gtgtgccttc caccagaac cggctg atg ggg aag 115

38 Met Gly Lys

39 1

41 tcg gag agc tca gtg ggg atg atg gag aga gcg gac aac tgt ggg agg 163

42 Ser Glu Ser Ser Val Gly Met Met Glu Arg Ala Asp Asn Cys Gly Arg

43 5 10 15

45 agg cgc cta ggc ttc gtg gag tgt ggg ctg ctg gta ctg ctg aca ctg 211

46 Arg Arg Leu Gly Phe Val Glu Cys Gly Leu Leu Val Leu Leu Thr Leu

47 20 25 30 35

49 ctg ttg atg gga gcc ata gtg act ctg ggt gtc ttc tac agc ata ggg 259

50 Leu Leu Met Gly Ala Ile Val Thr Leu Gly Val Phe Tyr Ser Ile Gly

51 40 45 50

53 aag cag ctg ccc ctc tta aat agc ctg ctg cac gtc tcc cgg cat gag 307

54 Lys Gln Leu Pro Leu Leu Asn Ser Leu Leu His Val Ser Arg His Glu

55 55 60 65

57 agg acg gtt gta aaa cga gtc ctc aga gat tca tcg cag aag agt gac 355

58 Arg Thr Val Val Lys Arg Val Leu Arg Asp Ser Ser Gln Lys Ser Asp

59 70 75 80

61 atc tgt act acc cca agc tgc gtg ata gca gct gcc aga atc ctc cag 403

62 Ile Cys Thr Thr Pro Ser Cys Val Ile Ala Ala Ala Arg Ile Leu Gln

63 85 90 95

65 aac atg gac cag tca aag aaa ccc tgc gac aac ttc tat cag tat gct 451

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66	Asn	Met	Asp	Gln	Ser	Lys	Lys	Pro	Cys	Asp	Asn	Phe	Tyr	Gln	Tyr	Ala	
67	100					105				110						115	
69	tgc	gga	ggc	tgg	cta	cgg	cac	cat	gtg	atc	ccc	gag	acc	aac	tcc	aga	499
70	Cys	Gly	Gly	Trp	Leu	Arg	His	His	Val	Ile	Pro	Glu	Thr	Asn	Ser	Arg	
71					120					125						130	
73	tac	agc	gtc	ttt	gac	atc	ctt	cgg	gat	gag	ctg	gag	gtc	atc	ctc	aaa	547
74	Tyr	Ser	Val	Phe	Asp	Ile	Leu	Arg	Asp	Glu	Leu	Glu	Val	Ile	Leu	Lys	
75					135					140						145	
77	ggg	gtg	ctg	gag	gat	tcc	tct	gtc	cag	cac	cgc	cca	gct	gtg	gag	aag	595
78	Gly	Val	Leu	Glu	Asp	Ser	Ser	Val	Gln	His	Arg	Pro	Ala	Val	Glu	Lys	
79			150						155					160			
81	gcc	aag	aca	ctg	tac	cgc	tcc	tgc	atg	aac	cag	agt	gtg	ata	gag	aag	643
82	Ala	Lys	Thr	Leu	Tyr	Arg	Ser	Cys	Met	Asn	Gln	Ser	Val	Ile	Glu	Lys	
83		165					170				175						
85	aga	gac	tct	gag	ccc	ctg	ctg	aac	gtc	tta	gat	atg	ata	gga	ggg	tgg	691
86	Arg	Asp	Ser	Glu	Pro	Leu	Leu	Asn	Val	Leu	Asp	Met	Ile	Gly	Gly	Trp	
87	180					185				190						195	
89	cct	gta	gcc	atg	gac	aag	tgg	aat	gag	acc	atg	ggc	ccc	aag	tgg	gaa	739
90	Pro	Val	Ala	Met	Asp	Lys	Trp	Asn	Glu	Thr	Met	Gly	Pro	Lys	Trp	Glu	
91					200					205					210		
93	ctg	gag	cgg	cag	ttg	gct	gtg	ttg	aac	tgc	cag	ttc	aac	agg	cgc	gtc	787
94	Leu	Glu	Arg	Gln	Leu	Ala	Val	Leu	Asn	Ser	Gln	Phe	Asn	Arg	Arg	Val	
95				215					220					225			
97	ctc	atc	gac	ctc	ttc	atc	tgg	aat	gat	gac	cag	aac	tcc	agc	cgg	cac	835
98	Leu	Ile	Asp	Leu	Phe	Ile	Trp	Asn	Asp	Asp	Gln	Asn	Ser	Ser	Arg	His	
99		230					235						240				
101	gtc	atc	tac	ata	gac	cag	ccc	acc	ttg	ggc	atg	ccc	tcc	cgg	gag	tac	883
102	Val	Ile	Tyr	Ile	Asp	Gln	Pro	Thr	Leu	Gly	Met	Pro	Ser	Arg	Glu	Tyr	
103		245				250					255						
105	tat	ttc	aag	gaa	gac	agc	cac	cgg	gta	cgg	gaa	gcc	tac	ctg	cag	ttc	931
106	Tyr	Phe	Lys	Glu	Asp	Ser	His	Arg	Val	Arg	Glu	Ala	Tyr	Leu	Gln	Phe	
107	260					265				270					275		
109	atg	aca	tca	gtg	gcc	act	atg	ctg	agg	aga	gac	ctg	aac	ctg	ccc	ggg	979
110	Met	Thr	Ser	Val	Ala	Thr	Met	Leu	Arg	Arg	Asp	Leu	Asn	Leu	Pro	Gly	
111					280					285				290			
113	gag	acc	gat	ttg	gtg	cag	gag	gaa	atg	gca	cag	gtg	ctg	cat	ctg	gag	1027
114	Glu	Thr	Asp	Leu	Val	Gln	Glu	Glu	Met	Ala	Gln	Val	Leu	His	Leu	Glu	
115				295					300					305			
117	aca	cat	ctg	gcc	aac	gcc	acg	gtc	ccc	cag	gag	aaa	agg	cat	gat	gtc	1075
118	Thr	His	Leu	Ala	Asn	Ala	Thr	Val	Pro	Gln	Glu	Lys	Arg	His	Asp	Val	
119			310					315						320			
121	acc	gcc	ctg	tat	cac	cga	atg	ggc	ctg	gag	gag	ctg	cag	gaa	agg	ttt	1123
122	Thr	Ala	Leu	Tyr	His	Arg	Met	Gly	Leu	Glu	Glu	Gln	Glu	Arg	Phe		
123		325					330						335				
125	ggg	ctg	aag	ggg	ttt	aac	tgg	act	ctc	ttc	ata	caa	aac	gtg	ctg	tct	1171
126	Gly	Leu	Lys	Gly	Phe	Asn	Trp	Thr	Leu	Phe	Ile	Gln	Asn	Val	Leu	Ser	
127	340				345					350					355		
129	tct	gtg	caa	gtt	gag	ctg	ctc	ccg	aat	gag	gag	gtg	gtg	gtc	tat	ggc	1219
130	Ser	Val	Gln	Val	Glu	Leu	Leu	Pro	Asn	Glu	Glu	Val	Val	Val	Tyr	Gly	

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131		360		365		370	
133	atc ccc tac ctg gag aat ctt gag gag atc att gac gtc ttc cca gca						1267
134	Ile Pro Tyr Leu Glu Asn Leu Glu Glu Ile Ile Asp Val Phe Pro Ala						
135		375		380		385	
137	cag acc ttg caa aac tac ctg gtg tgg cgc ctg gtg cta gat cgc atc						1315
138	Gln Thr Leu Gln Asn Tyr Leu Val Trp Arg Leu Val Leu Asp Arg Ile						
139		390		395		400	
141	ggc agc ctg agc cag aga ttc aaa gaa gcg cgt gtg gac tac cgc aag						1363
142	Gly Ser Leu Ser Gln Arg Phe Lys Glu Ala Arg Val Asp Tyr Arg Lys						
143		405		410		415	
145	gcg ctg tac ggt aca acc atg gag gaa gta cgc tgg cgg gag tgt gtc						1411
146	Ala Leu Tyr Gly Thr Thr Met Glu Glu Val Arg Trp Arg Glu Cys Val						
147	420		425		430	435	
149	agc tat gtc aac agc aac atg gag agt gcc gtg ggc tcc ctc tac atc						1459
150	Ser Tyr Val Asn Ser Asn Met Glu Ser Ala Val Gly Ser Leu Tyr Ile						
151		440		445		450	
153	aag cgg gcc ttc tcc aag gac agc aag agc ata gtc agt gag ctt atc						1507
154	Lys Arg Ala Phe Ser Lys Asp Ser Lys Ser Ile Val Ser Glu Leu Ile						
155		455		460		465	
157	gag aag ata cgg tcc gtg ttt gtg gat aac ctg gac gag ttg aac tgg						1555
158	Glu Lys Ile Arg Ser Val Phe Val Asp Asn Leu Asp Glu Leu Asn Trp						
159		470		475		480	
161	atg gat gag gaa tcc aag aaa aag gcc cag gaa aag gcc ttg aat atc						1603
162	Met Asp Glu Glu Ser Lys Lys Lys Ala Gln Glu Lys Ala Leu Asn Ile						
163		485		490		495	
165	cgg gaa cag atc ggc tac cct gac tac att ttg gaa gac aat aac aga						1651
166	Arg Glu Gln Ile Gly Tyr Pro Asp Tyr Ile Leu Glu Asp Asn Asn Arg						
167	500		505		510	515	
169	cac ctg gat gag gaa tac tcc agt ctg act ttc tca gag gac ctg tat						1699
170	His Leu Asp Glu Glu Tyr Ser Ser Leu Thr Phe Ser Glu Asp Leu Tyr						
171		520		525		530	
173	ttt gag aac ggg ctt cag aac ctc aag aac aat gcc caa agg agc ctc						1747
174	Phe Glu Asn Gly Leu Gln Asn Leu Lys Asn Asn Ala Gln Arg Ser Leu						
175		535		540		545	
177	aag aaa ctt cgg gaa aag gtg gac cag aat ctc tgg atc att ggg gct						1795
178	Lys Lys Leu Arg Glu Lys Val Asp Gln Asn Leu Trp Ile Ile Gly Ala						
179		550		555		560	
181	gca gtg gtc aat gca ttc tac tcc cca aac aga aac ctg atc gtc ttt						1843
182	Ala Val Val Asn Ala Phe Tyr Ser Pro Asn Arg Asn Leu Ile Val Phe						
183		565		570		575	
185	cca gcg ggg atc ctc cag cca ccc ttc ttc agc aag gac caa cca cag						1891
186	Pro Ala Gly Ile Leu Gln Pro Pro Phe Phe Ser Lys Asp Gln Pro Gln						
187	580		585		590	595	
189	gcc ttg aat ttc ggg ggc atc ggg atg gtg att gga cac gag atc aca						1939
190	Ala Leu Asn Phe Gly Gly Ile Gly Met Val Ile Gly His Glu Ile Thr						
191		600		605		610	
193	cac ggc ttt gat gat aac ggt cgg aac ttt gac aag aat ggc aac atg						1987
194	His Gly Phe Asp Asp Asn Gly Arg Asn Phe Asp Lys Asn Gly Asn Met						
195		615		620		625	

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198 Leu Asp Trp Trp Ser Asn Phe Ser Ala Arg His Phe Arg Gln Gln Ser
199      630      635      640
201 cag tgt atg att tat cag tac agc aac ttc tct tgg gaa cta gca gac      2083
202 Gln Cys Met Ile Tyr Gln Tyr Ser Asn Phe Ser Trp Glu Leu Ala Asp
203      645      650      655
205 aac cag aat gtg aac gga ttc agc acc ctc ggg gag aac atc gcc gac      2131
206 Asn Gln Asn Val Asn Gly Phe Ser Thr Leu Gly Glu Asn Ile Ala Asp
207 660      665      670      675
209 aac ggc ggt gtg cgg cag gca tac aag gct tac cta cag tgg cta gct      2179
210 Asn Gly Gly Val Arg Gln Ala Tyr Lys Ala Tyr Leu Gln Trp Leu Ala
211      680      685      690
213 gaa ggc ggc aga gac cag aga ctg ccg gga ctg aac ctg acc tat gct      2227
214 Glu Gly Gly Arg Asp Gln Arg Leu Pro Gly Leu Asn Leu Thr Tyr Ala
215      695      700      705
217 cag ctt ttc ttc att aac tat gcc cag gtg tgg tgt ggg tcc tac agg      2275
218 Gln Leu Phe Phe Ile Asn Tyr Ala Gln Val Trp Cys Gly Ser Tyr Arg
219      710      715      720
221 ccg gag ttc gcc atc cag tcc atc aag aca gat gtc cac agt cct ctt      2323
222 Pro Glu Phe Ala Ile Gln Ser Ile Lys Thr Asp Val His Ser Pro Leu
223      725      730      735
225 aag tac agg gtg ctg ggc tca cta cag aac cta cca ggc ttc tct gag      2371
226 Lys Tyr Arg Val Leu Gly Ser Leu Gln Asn Leu Pro Gly Phe Ser Glu
227 740      745      750      755
229 gcg ttc cac tgc cca cga ggc agc ccc atg cac cct atg aat cga tgt      2419
230 Ala Phe His Cys Pro Arg Gly Ser Pro Met His Pro Met Asn Arg Cys
231      760      765      770
233 cgc atc tgg tagccaaggc tgagctatgc tgcggcccccac gccccgccac      2468
234 Arg Ile Trp
237 ccagaggctt cgtgaatggt gtagccggca tagatgtgca gggtgttgcc tgaaggccac      2528
239 tggagccacc agccagccct ccgcgccag cctagagggc agccaccgc ccacatctgg      2588
241 gatgagtggg ggtgcctggt cctgcgcctt ttccggccag tgagggtcag cggcccggtg      2648
243 ggagcagtca gctgtccccc accctottca tagtgtgtgg ctaaatgtcc tcgagcttca      2708
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250 <211> LENGTH: 774
251 <212> TYPE: PRT
252 <213> ORGANISM: Rattus rattus
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258 Cys Gly Arg Arg Leu Gly Phe Val Glu Cys Gly Leu Leu Val Leu
259      20      25      30
261 Leu Thr Leu Leu Met Gly Ala Ile Val Thr Leu Gly Val Phe Tyr
262      35      40      45
264 Ser Ile Gly Lys Gln Leu Pro Leu Leu Asn Ser Leu Leu His Val Ser
265      50      55      60
267 Arg His Glu Arg Thr Val Val Lys Arg Val Leu Arg Asp Ser Ser Gln
268 65      70      75      80

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270 Lys Ser Asp Ile Cys Thr Thr Pro Ser Cys Val Ile Ala Ala Ala Arg
271      85      90      95
273 Ile Leu Gln Asn Met Asp Gln Ser Lys Lys Pro Cys Asp Asn Phe Tyr
274      100      105      110
276 Gln Tyr Ala Cys Gly Gly Trp Leu Arg His His Val Ile Pro Glu Thr
277      115      120      125
279 Asn Ser Arg Tyr Ser Val Phe Asp Ile Leu Arg Asp Glu Leu Glu Val
280      130      135      140
282 Ile Leu Lys Gly Val Leu Glu Asp Ser Ser Val Gln His Arg Pro Ala
283 145      150      155      160
285 Val Glu Lys Ala Lys Thr Leu Tyr Arg Ser Cys Met Asn Gln Ser Val
286      165      170      175
288 Ile Glu Lys Arg Asp Ser Glu Pro Leu Leu Asn Val Leu Asp Met Ile
289      180      185      190
291 Gly Gly Trp Pro Val Ala Met Asp Lys Trp Asn Glu Thr Met Gly Pro
292      195      200      205
294 Lys Trp Glu Leu Glu Arg Gln Leu Ala Val Leu Asn Ser Gln Phe Asn
295      210      215      220
297 Arg Arg Val Leu Ile Asp Leu Phe Ile Trp Asn Asp Asp Gln Asn Ser
298 225      230      235      240
300 Ser Arg His Val Ile Tyr Ile Asp Gln Pro Thr Leu Gly Met Pro Ser
301      245      250      255
303 Arg Glu Tyr Tyr Phe Lys Glu Asp Ser His Arg Val Arg Glu Ala Tyr
304      260      265      270
306 Leu Gln Phe Met Thr Ser Val Ala Thr Met Leu Arg Arg Asp Leu Asn
307      275      280      285
309 Leu Pro Gly Glu Thr Asp Leu Val Gln Glu Glu Met Ala Gln Val Leu
310      290      295      300
312 His Leu Glu Thr His Leu Ala Asn Ala Thr Val Pro Gln Glu Lys Arg
313 305      310      315      320
315 His Asp Val Thr Ala Leu Tyr His Arg Met Gly Leu Glu Glu Leu Gln
316      325      330      335
318 Glu Arg Phe Gly Leu Lys Gly Phe Asn Trp Thr Leu Phe Ile Gln Asn
319      340      345      350
321 Val Leu Ser Ser Val Gln Val Glu Leu Leu Pro Asn Glu Glu Val Val
322      355      360      365
324 Val Tyr Gly Ile Pro Tyr Leu Glu Asn Leu Glu Glu Ile Ile Asp Val
325      370      375      380
327 Phe Pro Ala Gln Thr Leu Gln Asn Tyr Leu Val Trp Arg Leu Val Leu
328 385      390      395      400
330 Asp Arg Ile Gly Ser Leu Ser Gln Arg Phe Lys Glu Ala Arg Val Asp
331      405      410      415
333 Tyr Arg Lys Ala Leu Tyr Gly Thr Thr Met Glu Glu Val Arg Trp Arg
334      420      425      430
336 Glu Cys Val Ser Tyr Val Asn Ser Asn Met Glu Ser Ala Val Gly Ser
337      435      440      445
339 Leu Tyr Ile Lys Arg Ala Phe Ser Lys Asp Ser Lys Ser Ile Val Ser
340      450      455      460
342 Glu Leu Ile Glu Lys Ile Arg Ser Val Phe Val Asp Asn Leu Asp Glu

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L:12 M:270 C: Current Application Number differs, Replaced Application Number

L:13 M:271 C: Current Filing Date differs, Replaced Current Filing Date